



NOV - 2 2011

Food and Drug Administration  
10903 New Hampshire Avenue  
Document Control Room - WO66-G609  
Silver Spring, MD 20993-0002

Mr. Joseph Mazzarella  
Sr. Manager Regulatory Affairs  
Edwards Lifesciences LLC  
One Edwards Way  
Irvine, CA 92614

Re: P100041  
Edwards SAPIEN™ Transcatheter Heart Valve, model 9000TFX, sizes 23mm and 26mm and accessories (RetroFlex 3™ Delivery System, models 9120FS23 and 9120FS26; RetroFlex™ Balloon Catheter, models 9120BC20 and 9120BC23; and Crimper, models 9100CR23 and 9100CR26)  
Filed: November 1, 2010  
Amended: December 27, 2010, March 1, 24 and 30, 2011, April 6, 14 and 19, 2011, May 2, 16 and 31, 2011, June 7, 8 and 15, 2011  
Prococode: NPT

Dear Mr. Mazzarella:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the SAPIEN™ Transcatheter Heart Valve, model 9000TFX, sizes 23mm and 26mm and accessories. This device is indicated for transfemoral delivery in patients with severe symptomatic native aortic valve stenosis who have been determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis. We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 2 years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" (please use this title even if the specified interval is more frequent than one year) and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the conditions outlined above, you must conduct two post-approval studies to: (1) continue the follow-up of patients from the premarket study through five years post-implant and (2) follow newly enrolled patients in a registry through five years post-implant.

1. *Continue Follow-up of Premarket Cohort:* This study should be conducted as per the protocol submitted as an attachment to your September 3, 2011 electronic mail message, Version 5.0. The objectives of this study are to describe the five-year durability and quality of life outcomes associated with use of the SAPIEN device. Durability will be evaluated using aortic insufficiency as measured via echocardiogram. Quality of life will be measured using the following assessments: Kansas City Cardiomyopathy Questionnaire (KCCQ), SF-12, and EuroQol (EQ)-5D Utilities. The surviving patients in the premarket cohort at the time of PMA approval will be followed annually up to 5-years.

2. *Newly Enrolled Study:* This study should be conducted as per the protocol submitted as an attachment to your September 2, 2011, Version 1.0. The objectives of this study are to evaluate: (1) the neurological and vascular outcomes at 30 days and annually through five years post-implant, (2) the learning curve among surgical teams placing the device at 50 geographically disbursed sites with high, moderate and low volumes of potential patient participation, and (3) composite safety and effectiveness endpoints at 30 days and annually through five years post-implant. Based on a background rate of 7.43% and censoring of 10% across the first year post-implant, it was calculated that a sample size of 1,100 patients is needed to have adequate power to assess the primary endpoint of neurological outcomes at one year post-implant. The data collection for this study (i.e. pre-procedure, peri-procedure, post-procedure, discharge, 30-day,

and 1-year follow-up) must be nested within the National Transcatheter Aortic Valve Replacement (TVT) registry housed jointly by the American College of Cardiology and Society for Thoracic Surgeons within four months of its initiation. You have also agreed to link the data to Centers for Medicare and Medicaid Services (CMS) data for long-term follow-up (annually through five years post-implant).

Within 30 days of your receipt of this letter, you must submit two separate PMA supplements that include the complete protocols of your two post-approval studies. Your PMA supplements should be clearly labeled as a "Post-Approval Study Protocol" and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" ([www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm#2)).

Please be advised that the results from these studies should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement.

FDA would like to remind you that you are required to submit separate PAS Progress Reports for each of the studies every six months during the first two years and annually thereafter. The reports should clearly be identified as Post-Approval Study Report. Two copies for each study, identified as "PMA Post-Approval Study Report" and bearing the applicable PMA reference number, should be submitted to the address below. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm>

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process"

([www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm](http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm)).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or
2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at [www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm](http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm).

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at [www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm](http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm).

CDRH does not evaluate information related to contract liability warranties. We remind you however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at [www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm](http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm). Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing. One of those three copies may be an electronic copy (eCopy), in an electronic format that FDA can process, review and archive (general information:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm134508.htm>; clinical and statistical data:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/ucm136377.htm>)

U.S. Food and Drug Administration  
Center for Devices and Radiological Health  
PMA Document Mail Center – WO66-G609  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Lisa Kennell at (301) 796-6376 or [lisa.kennell@fda.hhs.gov](mailto:lisa.kennell@fda.hhs.gov) (unofficial inquiries).

Sincerely yours,

*Christy Foreman*

Christy Foreman  
Director  
Office of Device Evaluation  
Center for Devices and  
Radiological Health



**Medical Device Tracking Order**

Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

NOV 02 2011

Mr. Joseph Mazzarella  
Sr. Manager Regulatory Affairs  
Edwards Lifesciences LLC  
One Edwards Way  
Irvine, CA 92614

RE: Edwards SAPIENT™ Transcatheter Heart Valve, model 9000TFX, sizes 23mm and 26mm and accessories (RetroFlex 3™ Delivery System, models 9120FS23 and 9120FS26; RetroFlex™ Balloon Catheter, models 9120BC20 and 9120BC23; and Crimper, models 9100CR23 and 9100CR26) (P100041)

Dear Mr. Mazzarella:

You are notified by this letter of your obligation to adopt a method of tracking for the device referenced above, as authorized by section 519(g) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 360i(g). The implementation of section 519(g) of the Act requires the Food and Drug Administration (FDA) to issue an order to manufacturers when FDA determines that a person who manufactures and distributes a device meets the relevant statutory requirements and tracking is required to protect the public health. This order is effective immediately.

Section 519(g) of the Act, states that FDA, “may by order require a manufacturer to adopt a method of tracking a class II or class III device—

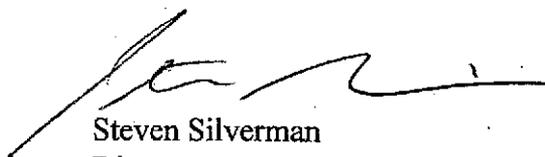
- (A) the failure of which would be reasonably likely to have serious adverse health consequences; or
- (B) which is—
  - (i) intended to be implanted in the human body for more than one year, or
  - (ii) a life sustaining or life supporting device used outside a device user facility.”

As you know, the corresponding medical device tracking regulations, found in Title 21 Code of Federal Regulations (CFR) Part 821, are intended to ensure that tracked devices can be traced from the device manufacturing facility to the person by whom the device is intended to be used when patient notification (under section 518(a) of the Act) or device recall (under section 518(e) of the Act) actions are ordered by the agency. The device tracking requirements for exemptions and variances, system and content requirements of tracking, the obligations of persons other than device manufacturers, records and inspection requirements, confidentiality, and record retention requirements, which were published in the Federal Register on August 16, 1993, remain in effect.

(21 CFR sections 821.2, 821.25, 821.30, 821.50, 821.55 and 821.60, copy enclosed)

This order to adopt a tracking method does not change your obligations concerning other existing FDA regulations affecting your device. FDA published in the Federal Register on February 28, 2002, an amendment to the final rule to revise the scope of the regulation and add certain patient confidentiality requirements and non-substantive changes to remove outdated references and simplify terminology. (67 FR 6943) If you need specific guidance, please contact Ann Ferriter, in the Office of Compliance, FDA Center for Devices and Radiological Health at (301) 796-5686. Other general information on your responsibilities under the Act, or more specific information, such as non-binding guidance on medical device tracking (copy enclosed), may be obtained from the Division of Small Manufacturers, International, and Consumer Assistance at its toll-free number (800) 638-2041, or at the internet address [www.fda.gov/cdrh](http://www.fda.gov/cdrh).

Sincerely yours,



Steven Silverman  
Director  
Office of Compliance  
Center for Devices and  
Radiological Health

Enclosures